Reactive Arthritis From Non-Antibiotic Related Clostridia Difficile Diarrhea

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Abstract

Most patients with Clostridium difficile infection manifest with only colonopathy and in fewer cases with extra colonic features (Clostridium difficile appendicitis, small bowel enteritis). In rare occasions extra intestinal involvement has been described such as cellulitis and reactive arthritis. Antibiotic use is the most important risk factor for Clostridium difficile infection, although it can occur without any identifiable risk factor. Since 1976 only few cases of clostridium difficile reactive arthritis have been reported and only 2 have been unrelated to antibiotics use. We report the first such case since 1998

INTRODUCTION

Most patients with Clostridium difficile infection manifest with only colonopathy and in fewer cases with extra colonic features (Clostridium difficile appendicitis, small bowel enteritis). In rare occasions extra intestinal involvement has been described such as cellulitis and reactive arthritis. Antibiotic use is the most important risk factor for Clostridium difficile infection, although it can occur without any identifiable risk factor. Since 1976 only few cases of clostridium difficile reactive arthritis have been reported and only 2 have been unrelated to antibiotics use. We report the first such case since 1998

CASE REPORT

A 61 year old African American male presented to Richmond University Medical Center with four weeks history of persistent non bloody diarrhea occurring 3-4 times daily. He had no associated nausea, vomiting, abdominal cramps or fever. He denied any recent travel, intake of undercooked meat, raw sea food, raw egg or use of antibiotics or chemotherapy in the past year. He had no change in his bowel habits prior to the onset of symptoms. He also complained of left knee pain and swelling for two days before admission. He denied any trauma, previous joint disease, extramarital sexual contact, bleeding abnormalities, photosensitivities, red eyes, urethral discharge, dysuria, rash, or mucus membrane lesions. His past medical history was significant for Diabetes mellitus, Hypertension, Asthma, Chronic Obstructive Pulmonary disease, Congestive Heart Failure, Cerebrovascular Accident, Chronic kidney disease and Cardiomyopathy. Current medications included glimepride, simvastatin, fluticasone/salmeterol, tiotropium, chlorothalidone, clopidogrel, bumetanide, diphenhydramine, doxazosin and insulin detemir.

Examination revealed an obese man in mild pain, with oral temperature of 99.3 F, respiratory rate of 20, pulse rate of 130 and blood pressure of 90/64mmHg. There was no evidence of conjunctivitis, rash or peripheral lymphadenopathy. The lungs were clear to both percussion and auscultation. The cardiac examination was normal except for a 3rd heart sound. There were no mormurs. There was truncal obesity with a soft, non-tender abdomen and no palpable organomegaly. The bowel sound was hyperactive. Peripheral pulses and neurologic exam were within normal limits. Musculoskeletal exam revealed left knee swelling, tenderness and pain limited range of motion. Hemoglobin was 11.1g/dl, hematocrit 35.2g/dl and white count 9.5 x 10^9/L with a normal differential. The sedimentation rate was 55mm in the first hour. Basic metabolic profile was within normal limit except for potassium of 3.1meq/L, blood urea nitrogen 29.2mg/dl, creatinine 2.5mg/dl. Liver function test and coagulation parameters were within normal limit. Rapid membrane enzyme immune assay of the stool revealed positive clostridium difficile antigen and toxin. The stool was negative for salmonella, shigella and campylobacter antigen. Knee X-ray showed no evidence of trauma; MRI revealed subcutaneous and deep tissue edema. The joint fluid analysis
both on presentation and repeat tap after 5 days (due to re-
accumulation) yielded no growth, no crystals, a rheumatoid 
factor of 8.0, WBC of 8044/cm³ and 1921/cm³ 
respectively. Multiple blood cultures were negative. Prior 
screening colonoscopy done two years ago ruled out the 
possibility of inflammatory bowel disease. 
Treatment included intravenous hydration, oral vancomycin, 
intravenous metronidazole, steroid for the arthritis. Empiric 
antisepsis with aztreonam and IV vancomycin which were 
discontinued after diagnosis of aseptic arthritis was made. 
The diarrhea resolved after 8 days but the effusion persisted 
for several days requiring a repeat tap. It slowly resolved 
four weeks after discharge.

**DISCUSSION**

Antibiotic use is the most widely recognized and modifiable 
risk factor for development of clostridium difficile 
infeciton2. Our patient belongs to the few patients that have 
non- antibiotic induced clostridium difficile associated 
diarrhea. Other established risk factors include 
hospitalization, advanced age, severe illness, gastric 
suppression3, enteral feeding, cancer chemotherapy, 
 hematopoietic stem cell transplant4, 5 none of which were 
present. Clostridium difficile infection associated diarrhea 
can still occur without any identifiable risk factor6. Only two 
cases of non-antibiotic related clostridium difficile reactive 
arthritis have been presently reported. 

Clostridium difficile enteral infections have rarely been 
reported as a cause of reactive arthritis compared to other 
enteric reactive arthritis (salmonella, shigella, Yersinia and 
campylobacter). Only few cases have been reported since 
the first recognized incidence in 1976. To the best of our 
knowledge, our case is the only case reported within the past 
4 years. Most of the cases reported so far involved more than 
one joint, though our patient had mono-articular 
volution. Migratory arthritis has also been reported8. 
The pathogenesis of clostridium reactive arthritis is still 
unclear. Reactive arthritis is usually ascribed to the presence 
of bacteria in extra-articular locations especially mucous 
membranes8. Presence of a bacterial component has been 
identified within the affected joint in chlamydia reactive 
arthritis9. Such finding has not been reported in clostridium 
reactive arthritis. Rather, immunoglobulin A antitoxin against 
the specific toxin of C. difficile has been found in the serum. 
The level of the antitoxin reflects the severity of the joint 
symptoms10. McCluskey et al. also found a neutralizing 
antitoxin in serum of his patient but not in synovial 
fluid.11The pathogenesis might also be similar to that 
suggested for intestinal bypass syndrome.12Two different 
and distinct toxins have been isolated from cultures of 
C. difficile. Toxin A enhances diarrhea and intestinal 
epithelial permeability, there by initiating immune complex 
deposit in the synovia. Toxin B is a virulent factor, 10 times 
more potent than A on a molar basis for mediating colonic 
damage13, 14. It is pertinent to mention that our patient had 
both toxin A and B. The MHC Class I allele HLA-B27 is 
associated with reactive arthritis secondary to enteric infections in approximately 50% of cases. HLA-B27 
positivity is associated with prolonged or severe 
oligoarthritis15. The role of HLA-B27 in presenting an 
arthritogenic epitope to CD8+ cells is supported by detection 
of oligoclonal T-cell expansion in patient with reactive 
arthritis.16 

Despite the rare occurrence of clostridium difficile reactive 
arthritis and the even rarer non antibiotic relationship, this 
organism should be considered in the etiology of long lasting 
but not permanent mono or polyarthritis

**References**


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